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CLINICAL RELEVANCE OF PAIN AND FUNCTION OUTCOMES IN GLUCOSAMINE SULFATE LONG-TERM TRIALS

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Aim of Study: The 2005 release of the Cochrane Review on glucosamine use in osteoarthritis outlined a moderate to large effect size on osteoarthritis symptoms in trials using the original crystalline glucosamine sulfate prescription preparation. Nevertheless, a small effect size was pointed out on WOMAC pain and function scores. Since the WOMAC index was used only in the two long-term 3-year trials with this formulation, we wanted to investigate whether the mild severity characteristics of the patients enrolled in such particular trials affected this effect size, and if the difference observed with placebo was in any case clinically relevant, besides being statistically significant.
Methods: Patients completing the 3-year treatment course in the randomised, double-blind, placebo-controlled trials of Reginster 2001 and Pavelka 2002, were pooled in a single database. The Minimal Clinically Important Improvement (MCII) and Patient Acceptable Symptom State (PASS) for WOMAC pain and function scores, were calculated according to Tubach 2005. The proportion of patients achieving such thresholds were compared between groups by the chi-square test.
Results: Out of the 259 completers (126 with placebo and 133 with glucosamine sulfate), over 50% were in PASS at the end of the studies regardless of treatment. However, they were 68.4% for WOMAC pain with glucosamine sulfate vs. 55.6% with placebo (p=0.033), and 63.9% vs. 50.0% on WOMAC function (p=0.024). Patients reporting MCII on WOMAC pain were 39.8% vs. 27.8%, respectively (p=0.040).
Conclusions: The mild severity characteristics of the patients enrolled in the two long-term trials with glucosamine sulfate allowed the vast majority of them to be in an acceptable symptom state, thus preventing the possibility of observing the moderate to large effect size for improvement that was reported in shorter studies. Nevertheless, there was a clinically relevant and significant difference of 10-15% in favor of glucosamine sulfate in the proportion of patients reaching MCII and PASS on pain and function.

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EVALUATION OF THE CLINICAL RELEVANCE OF THE SYMPTOMATIC EFFICACY OF LUMIRACOXIB IN OSTEOARTHRITIS UTILISING THE PATIENT ACCEPTABLE SYMPTOM STATE (PASS) CONCEPT

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Aim: The PASS is an absolute threshold value proposed for symptomatic variables in osteoarthritis (OA) to determine the point beyond which patients consider themselves well. The PASS differs from the baseline-dependent minimal clinically important difference. If the patient meets the PASS threshold, they achieve an acceptable symptom state regardless of their change from baseline in visual analogue scale (VAS) score. This makes the PASS a clinically relevant treatment target. In knee OA, PASS thresholds (on a 0–100 VAS scale) have been recently proposed as 32.3 mm for pain, 32.0 mm for patient's global assessment of disease activity and 31.0 mm for the WOMAC™ function subscale score. In previous analyses, lumiracoxib 100 mg once daily (od) was found to be significantly superior to placebo and non-inferior to celecoxib 200 mg od after 13 weeks in knee OA with respect to standard OA outcome variables. To assess the clinical relevance of these results from the perspective of the patient, the same data pooled from two large studies of knee OA were analyzed with respect to the PASS criteria for knee OA.
Methods: A total of 3235 patients were included in two multicenter, randomized, double-blind studies of identical design. Patients with an OA pain intensity in the target knee $\geq$40 mm on a 100 mm VAS were included; no flare was required. After a 3–7-day washout of previous NSAID/analgesic therapy, patients were randomized to receive lumiracoxib 100 mg od (n=811), lumiracoxib 100 mg od with a loading dose of lumiracoxib 200 mg od for the first two weeks (n=805), celecoxib 200 mg od (n=813) or placebo (n=806) for 13 weeks. The average effect of the two lumiracoxib 100 mg od regimens at 13 weeks was contrasted with the effects of celecoxib and placebo. Treatments were compared with respect to the PASS criteria (for OA pain, patient's global assessment of disease activity, and the WOMAC™ function [difficulty in performing daily activities] sub-scale score).
Results: Significant proportions of patients on lumiracoxib achieved a PASS (all three definitions) and lumiracoxib was significantly superior to placebo (all $p<0.05$).
Conclusion: PASS is an important concept in determining the clinical relevance of OA treatments. Percentages of patients on lumiracoxib 100 mg od who achieved a PASS were similar to those on celecoxib 200 mg od and significantly superior to those on placebo. This post-hoc analysis using PASS criteria suggests that the efficacy of lumiracoxib 100 mg od is of clinical relevance from the patient's perspective.

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A TWO-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL TO COMPARE THE EFFICACY OF LATERAL WEDGED INSOLES WITH SUBTALAR STRAPPING AND IN-SHOE LATERAL WEDGED INSOLES IN PATIENTS WITH VARUS DEFORMITY OSTEOARTHRITIS OF THE KNEE

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Aim of Study: In our previous study, we demonstrated that insoles with subtalar strapping (the strapped insole) maintained the valgus correction of the femorotibial angle (FTA) in patients with osteoarthritis varus deformity of the knee (knee OA) for six months. However, the six-month observation period was too short to evaluate the effect of the strapped insole on the progression of varus deformity of knee OA. Therefore, we continued to assess

Abstract P130 – Table 1. Percentage of patients achieving the PASS threshold criteria

PASS threshold criteria	Lumiracoxib 100 mg od (n=1616)	Celecoxib 200 mg od (n=813)	Placebo (n=806)
OA pain intensity (100 mm VAS) č32.3	44.3*	42.2*	35.4
Patient global assessment of disease activity (100 mm VAS) č32.0	43.3*	39.5*	32.7
WOMACTM function sub-scale score (100 mm VAS) č31.0	41.5*	38.6*	29.4

* $p<0.05$ vs placebo.

Abstract P131 – Table 1. Comparison of the FTA and Lequesne Index at baseline, month 6 and year 2.

	FTA (°)			Lequesne Index		
	Baseline	6-month	2-year	Baseline	6-month	2-year
Strapped insole group (n=21)	180.3±4.1	180.1±3.6	179.7±3.2	10.1±4.6	6.5±6.2	7.3±5.6
Inserted insole group (n=21)	180.8±4.6	180.8±4.2	182.4±4.7	9.7±4.2	8.6±5.5	9.6±4.8

the effect of the strapped insole on the FTA in patients with knee OA for two years.
Methods: The efficacy of the strapped insole and a traditional shoe insert wedged insole (the inserted insole), as a positive control, were compared at the baseline and after 2 years of treatment. Randomization was performed according to birth date. The 61 female outpatients with knee OA who completed the six-month study continued to receive treat with their respective insoles. The FTA was assessed by standing radiographs obtained while bare foot and the Lequesne index of knee OA at two years was compared with those at baseline in each insole group.
Results: There were 61 patients in the original study, but 19 (31.1%) withdrew. The 42 patients who completed the two-year study were evaluated. At the baseline assessment of the 42 patients, there was no significant differences in the FTA (P=0.73) or the Lequesne index (P=0.78), between the two groups. At the two-year assessment, the FTA was reduced by an average of 0.62°±2.6° in the strapped insole group (n=21), compared to the baseline assessment. However, the FTA was increased by 1.7°±3.5° compared with the period before the use of an insole in the inserted insole group (n=21). These changes represented a significant difference between the strapped and inserted insole groups (P=0.021). Compared with the initial assessment, the remission score, indicated by the Lequesne index at the two-year assessment, showed significantly greater improvement in the strapped insole group (-2.7±3.8) than in the inserted insole group (-0.14±4.1), (P =0.042).
Conclusion: In this study, only those participants using the subtalar strapped insole demonstrated no change in the femorotibial angle in comparison with the baseline assessments. If the insole with a subtalar strap maintains femorotibial angle for more than two years, it may restrict the progression of degenerative articular cartilage lesions of knee OA. We plan to continue monitoring our subjects for an additional 5 to 10 years in order to determine the long-term effect of the strapped insole.

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DYNAMIC JOINT LOADING ALTERATIONS ARE ASSOCIATED WITH RADIOGRAPHIC SEVERITY BUT NOT PAIN IN SUBJECTS WITH UNILATERAL HIP OSTEOARTHRITIS (OA)

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Introduction: Dynamic joint loading has been shown to be important in the pathophysiology of lower extremity osteoarthritis. Previous small studies have suggested that subjects with *end-stage* hip osteoarthritis (OA) have decreased peak external moments at the affected hip compared to normal subjects. However, whether these alterations are initiated early in the evolution of symptomatic hip OA or associated with the radiographic severity of hip OA is still not clear. The purpose of this investigation was to examine dynamic joint loading at the hips of subjects with varying degrees of radiographic and symptomatic unilateral hip OA.
Methods: 34 subjects with unilateral symptomatic hip OA and 16 age-matched normal subjects were evaluated. Subjects had mild to severe radiographic hip OA. Seven subjects had Kellgren Lawrence (KL) grade 1 hip OA, 8 had KL grade 2, 11 had KL grade 3, and 7 had KL grade 4 hip OA. Gait analyses were performed using an optoelectronic camera system and multi-component force plate. Inverse dynamics were used to calculate peak moments at the joints and determine range of motion at the joints. Pain was assessed using the Western Ontario MacMasters Universities Osteoarthritis Index (WOMAC™). Spearman correlations were used to correlate peak moments with KL grade and pain at the affected hip. Independent samples t-test were used to compare normal subjects with the hip OA subjects.
Results: Significant correlations were found between dynamic joint loads and KL grade at the affected hip. KL grade was inversely correlated with the peak hip flexion moment (rho=-0.554, p=0.001), hip internal rotation moment (rho=-0.580, p=0.001), hip extension moment (rho=-0.386, p=0.05) and hip range of motion (rho=-0.698, p<0.001). There was no correlation between peak hip moments and pain at the affected hip. There was also no significant correlation between KL grade at the affected hip and peak moments at the contralateral hip. When comparing subjects with mild to moderate unilateral hip OA (KL grade 1 through 3) with normal subjects, the hip OA subjects had significantly lower peak hip flexion (p=0.016), adduction (p<0.001), and internal rotation moments (p=0.05). Interestingly, these subjects also had significantly lower peak *knee* extension (p=0.032) and *knee* adduction moment (p=0.013) at the ipsilateral limb compared to normal subjects.
Conclusion: Subjects with unilateral hip OA have lower peak dynamic loads at the affected hip and ipsilateral knee when compared to normal subjects. This decrease in joint loads occurs early in the course of unilateral hip OA and is correlated with radiographic severity of hip OA. Furthermore, this decrease in joint loads appears to be independent of pain at the affected hip. Future studies should evaluate what factors may contribute to these alterations in loading and how these alterations may influence the progression of lower extremity OA in these subjects.

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ORAL CALCITONIN PROTECTS AGAINST EXPERIMENTIALLY INDUCED OSTEOARTHRITIS

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Purpose: To investigate whether oral calcitonin treatment influences the rise in cartilage degradation accompanying estrogen deficiency, and whether calcitonin has any direct effects on chondrocytes in this context.
Methods: Fifty rats aged seven months were randomly allocated into five intervention groups. Rats undergoing bilateral ovariectomy (OVX) were used to mimic the hormonal status characteristic for the menopause. The five intervention groups were as follows: 1) Sham, 2) OVX, 3) OVX+estrogen, 4) OVX+2mg/kg calcitonin plus 50mg/kg 5-CNAC, and 5) OVX + 50mg/kg 5-CNAC. Each treatment was administered for six weeks after OVX. Fasting blood samples for biomarker analysis were taken at baseline, day 3, and weeks 1, 2, 4, and 6. Cartilage degradation was quantified by measuring the changes in the concentration of C-telopeptides of collagen type II (CTX-II ELISA), and the changes in the severity scores of articular cartilage erosions visualized in